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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/628,909	07/29/2003	Lawrence S. Barak	186550/US/4	8116

32940 7590 04/19/2007  
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EXAMINER
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BASI, NIRMAL SINGH

ART UNIT	PAPER NUMBER
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1646

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	04/19/2007	PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

<b>Office Action Summary</b>	<b>Application No.</b> 10/628,909	<b>Applicant(s)</b> BARAK ET AL.	
	<b>Examiner</b> Nirmal S. Basi	<b>Art Unit</b> 1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) ☒ Responsive to communication(s) filed on 1/31/07.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) ☐ Claim(s) 1-3, 17-77 and 84-87 is/are pending in the application.
- 4a) Of the above claim(s) 17-77 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☐ Claim(s) 1-3 and 84-87 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 27 August 2004 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)   | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)   | 5) <input type="checkbox"/> Notice of Informal Patent Application                       |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)<br>Paper No(s)/Mail Date <u>4/8/05, 7/29/03</u> . | 6) <input type="checkbox"/> Other: _____  |

### **DETAILED ACTION**

1. The Amendments filed 4/8/05 and 1/31/07 have been entered. The Oath or Declaration filed 4/7/05 has been entered. Response to Restriction requirement filed 1/31/07 has been entered.
2. Applicants response to Pre-Exam formalities filed 8/27/04 has been entered.

### ***Election/Restriction***

Applicant's election without traverse of Group I (drawn to a conjugate comprising a  $\beta$ -arrestin and a detectable molecule), claims 1-3, on 1/31/07 is acknowledged. Applicant had added new claims 84-87, cancelled claims 4-16 and 78-83. Amended claims 1-3 and newly added claims 84-87 will be examined as they pertain to the elected invention of Group I. Claims 17- 77 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b) as being drawn to a non-elected. The requirement is still deemed proper and is therefore made FINAL.

3. IDSs filed 7/29/03 and 4/8/05 have been considered.

### ***Specification***

The disclosure is objected to because of the following informalities:

4. An application in which the benefits of an earlier application are desired must contain a specific reference to the prior application(s) in the first sentence of the specification (37 CFR 1.78) as well as the relationship of instant application to the parent. Parent Application 09/631,468, is now abandoned, and must be indicated as such.

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In the "Brief Description of the Drawings" each panel of Figure 4 must be described separately, i.e. as Figure 4A and Figure 4B and not as Row A and Row B. Similarly, Figure 5 must be described as Figure 5A and Figure 5B and not as Row A and Row B. Appropriate correction is required.

***Drawings***

5. The drawings filed on 8/27/04 are approved by the Examiner.

***Claim Rejections - 35 USC § 101***

6. 35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1-2 and 85 and 87 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter.

Claims 1-2 and 85 and 87 recite a conjugate but do not recite that conjugate is isolated or purified. It must be noted that  $\beta$ -arrestins exist as conjugates with receptors in nature. The claims as currently recited encompass these naturally-occurring compounds. Therefore, the conjugates as claimed are a product that occurs in nature and does not show the hand of man, and as such is non-statutory subject matter. It is suggested that the claims be amended to recite "an isolated and purified" to overcome this rejection.

***Claim Rejections - 35 USC § 112 (second paragraph)***

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make

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and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-2 and 84-87 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 2 is indefinite with respect to the term "optically detectable". It is not clear which molecules are considered "optically detectable" and which are considered not "optically detectable" so as to allow the metes and bounds of the claim cannot be determined. It is not clear if optically detectable means by detecting directly by looking at the molecule, looking at it through a microscope, on an X-ray film etc. so as to allow the metes and bounds of the claim to be determined. The molecules that are considered optically detectable are not defined. The definition of optically detectable labels is not provided.

Claim 1 is indefinite with respect to the term "label". It is not clear what is considered a label with respect to the conjugate claimed. A label can be a slip (as in paper or cloth) inscribed and affixed to something for identification or description. Without a clear definition of "label" as it pertains to the molecules or compounds encompassed by the claim the metes and bounds of the claim cannot be determined.

Claims 2 and 84-87 are indefinite because the metes and bounds of the fluorescent label, colorimetric label, radioactive label and electron-dense label cannot be determined because the term "label" is considered indefinite for reasons given above.

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The term "electron-dense" in claim 87 is a relative term which renders the claim indefinite. The term "electron-dense" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. It is not clear when a label is considered electron-dense as compared to a label not being considered electron-dense. What is the cut-off level for density when one label transitions from electron dense to not electron dense. What is the minimum number of electron required for a label to be considered electron-dense.

#### **Claim Rejections, 35 U.S.C. 102**

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

8. Claims 1, 2 and 84-87 are rejected under 35 U.S.C. 102(a) as being anticipated by Goodman et al (IDS Ref, Nature, 338:447-450, 1996). Goodman disclose conjugate comprising  $\beta$ -arrestin covalently linked to arrestin. (page 448, see Fig 3, pages 449-450, see Methods and page 447, see columns 1 and 2). The label for the conjugate comprises arrestin which is an optically detectable

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molecule. Goodman also discloses [ $^3\text{H}$ ] leucine labeled  $\beta$ -arrestin constructs (page 449), commassie blue stained  $\beta$ -arrestin (Fig 2) and immunoblotting using anti-  $\beta$ -arrestin antibodies using chemiluminescence. Therefore Goodman discloses a conjugate comprising  $\beta$ -arrestin and label, wherein the label is optically detectable, fluorescent, colorimetric, radio-active and electron-dense thereby meeting the limitation of claims 1, 2, 84-87, absent evidence to the contrary.

9. Claims 1-2, 85 and 87 are rejected under 35 U.S.C. 102(b) as being anticipated by Zuckerman, R et al (IDS Ref, FEBS Let, 238(2):379-84 (1980)). Zuckerman discloses  $\beta$ -arrestin covalently linked to PDE and rhodopsin, see Abstract. The conjugate of Zuckerman comprises  $\beta$ -arrestin and an optically detectable molecule, electron-dense label and a colorimetric label thereby meeting the limitation of claims 1, 2, 85 and 87, absent evidence to the contrary.

10. Claim 1, 2 and 85-87 and dependent claim 2 are newly rejected under 35 U.S.C. 102(b) as being anticipated by Gurevich et al (IDS Ref, JBC, Vol. 368, No. 23, pages-16879-16882, 1993). Gurevich discloses the [ $^3\text{H}$ ] leucine labeled  $\beta$ -arrestin constructs generated in an *in vitro* translation system thereby meeting the limitation of claims 1, 2 and 85-87, absent evidence to the contrary.

### **Claim Rejections, 35 U.S.C. 103**

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

11. Claim 3 is rejected under 35 U.S.C. 103(a) as being unpatentable over Chalfie et al (IDS, Ref. US Patent 5, 491,084) in view of Zuckerman et al (IDS Ref, FEBS Let, 238(2):379-84 (1980) or Goodman et al (IDS Ref, Nature, 338:447-450, 1996) or Gurevich et al (IDS Ref, JBC, Vol. 368, No. 23, pages-16879-16882, 1993).



Chalfie et al. disclose various uses of green-fluorescent protein and provide a method for selecting cells expressing a protein of interest which comprises: a. introduction into the cells a DNAI molecule having DNA sequence encoding the protein of interest and DNAll molecule having DNA sequence encoding a green-fluorescent protein; b. culturing the introduced cell in conditions permitting expression of the green-fluorescent protein and the protein of interest ; and selecting the cultured cells which express green-fluorescent protein (see abstract). Also disclosed is a method of localizing a protein of interest in a cell, said protein encoding the protein of interest linked (fusion protein, conjugated protein) to green-fluorescent protein. (See summary of Invention, column 1). The green-fluorescent protein can be used in cells such as: bacterial cells, yeast cells, fungal cells, insect cells, nematode cells, plant cells, Vero cells , HeLa cells, COS cells, CV1 cells and various primary mammalian cells (column 2, lines 30-35); and in different tissues (column 5, line 56-67). The cells and organisms may be used to detect the presence of different molecules in various kinds of biological samples (column 4, lines 13-23). Chalfie et al. does not teach the conjugation of  $\beta$ -arrestin protein to green-fluorescent protein

Zuckerman, Goodman and Gurevich all discloses the production of  $\beta$ -arrestin conjugates and uses said conjugates to identify the target proteins for  $\beta$ -arrestin action. The teachings of Zuckerman, Goodman and Gurevich are disclosed above. It would have been prima facie obvious to a person of ordinary skill in the art at the time the invention was made to use the green fluorescent protein taught by Chalfie et al and conjugate it to  $\beta$ -arrestin taught by

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Zuckerman, Goodman or Gurevich to construct a detectible molecule to be used in the identification of target proteins for  $\beta$ -arrestin action.

The ordinary artisan would have been motivated to produce a green fluorescent protein conjugated to  $\beta$ -arrestin to function as a reporter molecule to monitor the effect of  $\beta$ -arrestin targeting in cells because Chalfie states GFP conjugates can be used to localize proteins in living cells, see column 1. Since, the art of the art at the time of filing instant application was investigating  $\beta$ -arrestin signaling and localization in the cell, the motivation to create labeled  $\beta$ -arrestin clearly existed.

The ordinary artisan would have expected success at producing the optically detectible conjugate using an active green fluorescent protein conjugated to  $\beta$ -arrestin as a reporter molecule for interaction with protein localization inside a cell because other active optically active  $\beta$ -arrestin conjugated proteins involved in signal transduction were routinely produced.

12. No claim is allowed.

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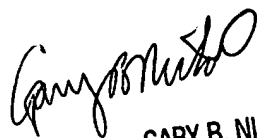
Advisory

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nirmal S. Basi whose telephone number is 571-272-0868. The examiner can normally be reached on 9:00 AM-5:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Nickol can be reached on 571-272-0835. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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